8M

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/763,308 | 02/20/2001 | Per-Ola Arvidsson | 06275-228001 | 5091 |

26161 7590 04/28/2004

FISH & RICHARDSON PC
225 FRANKLIN ST
BOSTON, MA 02110

| EXAMINER | |
|---|---|
| EPPERSON, JON D | |
| **ART UNIT** | **PAPER NUMBER** |
| 1639 | |

DATE MAILED: 04/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/763,308 | ARVIDSSON ET AL. | |
| | Examiner | Art Unit | |
| | Jon D Epperson | 1639 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *17 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *12-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/6/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Status of the Application*

1. The Response filed February 17, 2004 is acknowledged.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### *Status of the Claims*

3. Claims 1-14 were pending. Applicants amended claim 1. Therefore claims 1-14 are currently pending.

4. Claims 12-14 are drawn to non-elected species and/or inventions and thus these claims remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), there being no allowable generic claim.

5. Therefore, claims 1-11 are examined on the merits in this action.

6. This application contains claims 12-14 drawn to a nonelected invention(s). This was addressed in the previous action (see Paper No. 8, paragraph 4). A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

## Withdrawn Objections/Rejections

7. The Written Description rejection under 35 U.S.C. 112, first paragraph is withdrawn in view of Applicants' arguments and/or amendments. The Tabushi, Castillo and Nishiki rejections under 35 U.S.C. § 102 are withdrawn in view of Applicants' amendments and/or arguments. The rejections under 35 U.S.C. § 103 are withdrawn in view of Applicants' amendments and/or arguments. All other rejections are maintained and the arguments are addressed below.

## Outstanding Objections and/or Rejections

### *Claims Rejections - 35 U.S.C. 112, first paragraph*

8. Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a few of the compounds that fall within the broad scope of the claimed invention (see below), is not enabling for the vast majority of compounds that fall within this broad scope. This is an enablement rejection.

> Any person skilled in the art to which it pertains, or with which it is most nearly connected, would not know how to make and use the claimed invention. Applicant has not provided enough examples of how to use the claimed invention to be enabling for the full breadth of the claims. It is clear from applicants' specification and the teachings of the prior art how one might practice this invention with a library of compounds that can "enter the cyclodextrin cavity", which is the art recognized mechanism by which cyclodextrins protect their respective ligands (e.g., see Tabushi et al., page 1023, Scheme I, compound 18 showing encapsulation of a quinone by a cyclodextrin which afford

protection to the quinone from oxidation). However, applicants have not provided sufficient guidance as to how to make/use **any** of the other compounds that not enter the cyclodextrin cavity and/or bind to the cyclodextrin cavity at all.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include, but are not limited to:

(1) the breadth of the claims;
(2) the nature of the invention;
(3) the state of the prior art;
(4) the level of one of ordinary skill;
(5) the level of predictability in the art;
(6) the amount of direction provided by the inventor;
(7) the existence of working examples; and
(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(1-2) Breadth of the claims and nature of the invention: The breadth of the claims is large because it includes all compounds and hence reads on an infinite number of possibilities and, as a result, the nature of the invention cannot be determined for such broad scope.

(3 and 5) The state of the prior art and the level of predictability in the art: The prior art teaches that **ONLY** compounds that can enter the cyclodextrin cavity will be afforded some level of protection. However, Applicants claims include a large number of compounds (indeed the majority of Applicants' claimed compounds) that would not fall within this class of compounds. Therefore, the level of predictability in the prior art for those compounds is low or absent.

(4) The level of one of ordinary skill: The level of skill required would be high, most likely at the Ph.D. level.

(6-7) The amount of direction provided by the inventor and the existence of working examples: Applicants have not provided any guidance on how to use their invention with a library of compounds that do not enter the cyclodextrin cavity and/or at least bind to the cyclodextrin. Therefore, the Examiner contends that the vast majority of Applicants' claimed embodiments are inoperative.

(8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: The instant specification for all the reasons asserted above does not provide to one skilled in the art a reasonable amount of guidance to use the claimed invention with compounds that do not enter the cyclodextrin cavity. It would take undue experimentation to determine (1) which compounds would enter the cyclodextrin cavity and (2) for those compounds that do not, which would include the vast majority of the compounds that would fall within the scope of Applicants' claims, the invention just doesn't work i.e., if there is no interaction – there can be no protection. Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. *In re Vaeck*, 947 F.2d 488, 496 & n.23, 20 USPQ2d 1438, 1445 & n.23 (Fed. Cir. 1991). Therefore, it is deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed. Thus, due to the inadequacies of the instant disclosure, one of ordinary skill would not have a reasonable expectation of

success and the practice of the full scope of the invention would require undue experimentation.

***Response***

9. Applicant's arguments directed to the above Enablement rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

**[1]** Applicants restate the limitations in the claims (e.g., claims 1-11) but do not refute the Examiner's arguments that the nature of the invention is "undeterminable" and that the claims are very "broad" in scope (e.g., see 2/17/2004 Response, "Nature of the invention" and "Breadth of claims" section).

**[2]** Applicants argue that the level of one of ordinary skill in the art is a Ph.D. (e.g., see 2/02/2004 Response, page 6, "Level of one of ordinary skill" section).

**[3]** Applicants admit that the state of the prior art provides little or no guidance (e.g., see 2/02/2004 Response, page 6, "State of the prior art" section) and further admit that the art is unpredictable (e.g., see 2/17/2004 Response, page 6, "Level of predictability in the art" section, "The relevant art is generally unpredictable") (emphasis added).

**[4]** Applicants argue that they have provided enough working examples to enable the claimed invention and cite their 80 compound library and 1600 compound library (e.g., see 2/02/2004 Response, page 6 referring to Examples 1-2 in the specification). Applicants further

argue that the specification (e.g., page 3, lines 20-27) would provide sufficient guidance to enable the full scope of the claims (see 2/17/2004 Response, paragraph bridging pages 6-7).

**[5]** Applicants conclude that undue experimentation would not be required (e.g., see 2/17/2004 Response, page 7, "quantity of experimentation needed" section).

This is not found persuasive for the following reasons:

**[1]** The Examiner contends that Applicants concede Wands factors (1 and 2) by failing to provide any arguments to rebut the Examiner's assertions that the claims are unduly broad (see rejection above).

**[2]** The Examiner concedes Wands factor (4) as set forth in the original rejection.

**[3]** The Examiner contends that Applicants concede Wands factors (3 and 5) by admitting that there is little or no guidance and that the art is unpredictable.

**[4]** The Examiner contends that no structures have been provided for the library members and, as a result, the examples are entirely illusory. In addition, the Examiner notes that Applicants have not refuted the Tabushi et al. reference which clearly shows that the cyclodextrins will NOT work unless there is host-guest chemistry employed (i.e., nothing in Applicants' specification teaches how one might practice this invention with a library of compounds that can't "enter the cyclodextrin cavity", which is the art recognized mechanism by which cyclodextrins protect their respective ligands). Applicants' recited passages provide only general guidance (e.g., a laundry list of "potential" compounds) and do not even address the issue of host-guest chemistry set forth in Tabushi et al. Thus, the Examiner contends that Applicants concede Wands factors (6-7).

**[5]** The Examiner contends that majority of Wands factor (e.g., 1-3 and 5-8) indicate that undue experimentation would be required (see above).

Accordingly, the Enablement rejection cited above is hereby maintained.

***Claims Rejections - 35 U.S.C. 102***

10. Claims 1-11 are rejected under 35 U.S.C. 102(a) as being anticipated by Henco et al. (EP 0 947 820 A2) (Date of Publication is **October 6, 1999**).

For ***claims 1-11***, Henco et al. (see entire document) discloses the use of cyclodextrins (including Applicant's elected 2-hydroxypropyl-β-cyclodextrin, see claim 7) as additives for compound storage, which anticipates claims 1-11. Please note that the additive is first combined to a solution of the compounds and thus is also prepared (at least for a while) in a wet form. Furthermore, Henco et al. disclose 4% by weigh which falls within applicants' claimed specification range (see Henco, claim 8; see also page 4 of Applicants' specification for conversion chart from %wt to mM concentration). Furthermore, Henco et al. disclose that the cyclodextrin can be applied to libraries that contain hundreds of thousands of compounds like the ones typically used in high throughput screening (e.g., see page 2, line 6; see also page 3, line 39; see also page 4, line 9; see also figures).

***Response***

11. Applicant's arguments directed to the above 35 U.S.C. § 102 rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Applicants argue that Henco should not be considered prior art because Applicants foreign priority date (i.e., August 24, 1999) is before the publication date of Henco (i.e., October 6, 1999). Furthermore, Applicants argue that the IB should provide the Swedish priority document (e.g., see 2/17/2004 Response, footnote 2).

This is not found persuasive for the following reasons:

The Examiner contends that Henco is prior art because Applicants priority foreign priority request has not been granted. Applicants and/or the IB have not sent a certified copy to the USPTO nor has a translation of said certified copy been provided (e.g., see MPEP § 201.15). Therefore, Applicants arguments are moot.

Accordingly, the 35 U.S.C. 102 rejection cited above is hereby maintained.

## New Rejections and/or Objections

### *Claim Rejections - 35 USC § 103*

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1-9 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Szente et al. (Szente, L.; Harangi, J.; Szejtli, J. "Long term storage stability studies on flavour β-cyclodextrin complexes" Proc. Int. Symp. Cyclodextrins, 4th (1988), 545-9. Editor(s): Huber, O.; Szejtli, J. Kluwer: Dordrecht, Neth.) and Tabushi et al. (Tabushi, I.; Yamamura, K.; Fujita, K.; Kawakubo, H. "Specific Inclusion Catalysis by β-Cyclodextrin in the One-Step Preparation of Vitamin K1 or K2 Analogues" *J. Am. Chem. Soc.* **1979**, *101(4)*, 1019-1026) and Applicants' admission in the Specification.

For ***claims 1***, Szente et al. (see entire document) disclose adding β-cyclodextrin to a library of natural and synthetic flavors to prevent degradation for periods as long as 10 years (see Szente et al., Summary), which reads on claim 1. Although Szente et al. do not

explicitly state that they are adding cyclodextrin to a library with "at least 100 compounds", each of the 21 "flavors" listed in Table 1 contains ~10-20 compounds (e.g., see figures 1 and 2 wherein for (1) Garlic and (2) Dill "flavors" contain approximately ~32 compounds exemplified by the ~19 and ~13 large and small peaks shown in the chromatographs, respectively) and, as a result, a library of approximately 21 × ~10-20 compounds is generated (i.e., a library of approximately 200 to 400 compounds). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The Office does not have the facilities to make such a comparison and the burden is on the applicants to establish the difference. See *In re Best,* 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.). Thus, the flavors listed in Table I inherently contain >100 compounds and, in addition, more "flavors" and thus more compounds would be immediately envisioned by a person of skill in the art. Furthermore, Szente et al. disclose storing each of said compounds in cyclodextrin for periods as long as 10 years (e.g., see Szente et al., Table 1).

For ***claim 4***, Szente et al. disclose compounds like benzaldehyde, which represents an organic compound that is less than 1000 Daltons i.e., MW is ~106 (e.g., see Table 1).

For ***claim 11***, Szente et al. disclose storing in "normal humidity" which reads on a "wet form" (e.g., see Szente et al., Experimental Section).

The prior art teaching of Tabushi et al. differs from the claimed invention as follows:

For ***claim 1, 5-9***, the prior art teachings of Szente et al. do not specifically recite the use of 20-200mM concentration of cyclodextrin. The reference is silent on this issue (i.e., no cyclodextrin concentration is given).

For ***claims 2-3***, the prior art teachings of Szente et al. differ from the claimed invention by not specifically reciting the use of a library comprising at least 1000 or 10000 members.

However, Specification teaches the following limitations that are deficient in Tabushi et al.:

For ***claims 1, 4-9 and 11***, Tabushi et al. (see entire document) discloses adding β-cyclodextrin to a library of Vitamin K analogues to prevent them from $H_2O_2$ attack (see Tabushi et al., page 1023, scheme I showing protection of compound(s) **18** from $H_2O_2$ attack; see also page 1020, column 2, compounds 7 and 8 wherein the R groups are defined; please note that the Vitamin K analogs are less than 1000 Da). Furthermore, Tabushi et al. disclose using a 50mM concentration of β-cyclodextrin and also discloses varying the concentration of β-cyclodextrin in relation to the compounds in the library and, as a result, would anticipate any other concentration as well (see Tabushi et al., page 1020, Table 1, superscript "a" denoting the β-cyclodextrin concentration at "$5 \times 10^{-2}$ M"; see also column 2, paragraph 1).

For ***claims 2-3***, the Specification teaches that compound libraries may contain more than 100,000 different compounds and can be used in high throughput screening

(see Specification, paragraph 2-3; see especially paragraph 2, lines 10-11, "Compound libraries may for example contain more than 100,000 different compounds").

It would have been obvious to one skilled in the art at the time the invention was made to use the 50 mM concentration of cyclodextrin as taught by Tabushi et al. for the storage of the natural and synthetic flavor compounds as taught by Szente et al. because both references use cyclodextrin to protect libraries of compounds (i.e., the references represent analogous art). Furthermore, a person of ordinary skill would have been motivated to combine the references because Tabushi et al. teach that phenolic compounds can be protected using cyclodextrin at 50 mM concentration, which would extend to the phenolic compounds disclosed by Szente et al. (e.g., see Tabushi et al, scheme I outlining mechanism for protecting phenolic compounds; see also Szente et al. wherein phenolic compounds are disclosed).

In addition, it would be conventional and within the skill of the art to *identify the optimal concentration*. It is well-established that merely selecting proportions and ranges is not patentable absent a showing of criticality. In re Becket, 33 U.S.P.Q. 33 (C.C.P.A. 1937). In re Russell, 439 F. 2d 1228, 169 U.S.P.Q. 426 (C.C.P.A. 1971). See also MPEP 2144.05 II.A., "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. '[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.' In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between

40C and 80C and an acid concentration between 25 and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100C and an acid concentration of 10%.).

In addition, it would have been obvious to screen larger libraries than the ones taught by Szente et al. and Tabushi et al (i.e., libraries with more than 100,000 compounds) with the β-cyclodextrins because the Specification admits that larger libraries can be used for screening purposes which would include the biological (e.g., tast screening) and/or pharmaceutical screening set forth by the Szente et al. and Tabushi et al. references. Furthermore, one of ordinary skill in the art would have been motivated to use β-cyclodextrins with larger libraries of susceptible phenolic compounds to protect more compounds from potential $H_2O_2$ attack and/or other forms of degradation before screening.

***Response***

15. Applicant's arguments directed to the above 35 U.S.C. § 103(a) rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

**[1]** Applicants argue that Tabushi does not disclose the compound libraries covered by claims 1-9 and 11 (e.g., see 2/17/2004 Response, page 8, paragraph 2).

**[2]** Applicants argue that there is no suggestion to modify Tabushi to render obvious the claimed invention and that the mere fact that compound libraries were known in the art at the

time of filing is not in and of itself sufficient motivation. Furthermore, Tabushi appears to disclose only five compounds in cyclodextrin (e.g., see 2/17/2004 Response, page 8, paragraph 2), which does not meet the "at least 100" compound limitation in newly amended claim 1.

This is not found persuasive for the following reasons:

**[1]** The Examiner contends that Szente does disclose a compound library that reads on claim 1 (e.g., see Table I) and that the specification makes up for the deficiencies in claims 2-3.

**[2]** The Examiner contends that Szente et al. do disclose a compound library with >100 compounds and, as a result, Applicants arguments are moot for claim 1. In addition, the Examiner respectfully disagrees with Applicants that there is no motivation to protect larger libraries with cyclodextrin because it would always be obvious to protect as many compounds from degradation as possible. In addition, Applicants admit in their specification that libraries of greater than 10,000 compounds were routinely screened in the art at the time of filing and, as a result, a person of skill in the art would be motivated to protect larger libraries for screening purposes, which is exactly what the libraries disclosed by Szente et al. (i.e., screening for taste) and Tabushi et al. (screening for pharmaceutical activity) are used for.

16. Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Szente et al. (Szente, L.; Harangi, J.; Szejtli, J. "Long term storage stability studies on flavour β-cyclodextrin complexes" Proc. Int. Symp. Cyclodextrins, 4$^{th}$ (1988), 545-9. Editor(s): Huber, O.; Szejtli, J. Kluwer: Dordrecht, Neth.) and Tabushi et al (Tabushi, I.; Yamamura, K.; Fujita, K.; Kawakubo, H. "Specific Inclusion Catalysis by β-Cyclodextrin in the One-Step Preparation of Vitamin K1 or

K2 Analogues" *J. Am. Chem. Soc.* **1979**, *101(4)*, 1019-1026) and Castillo et al (U.S. Patent No. 5,985,310) (102(e) Date is ***March 10, 1998***) and Applicants' admission in the specification.

For ***claims 1-9 and 11***, the combined teachings of Szente et al., Tabushi et al., and the specification render obvious claims 1-9 and 11 (see 35 U.S.C. 103(a) rejection above, which is incorporated in its entirety herein by reference).

The combined prior art teaching of Szente et al., Tabushi et al. and the specification differ from the claimed invention as follows:

For ***claim 10***, the combined prior art teachings of Szente et al., Tabushi et al., and the specification differ from the claimed invention by not specifically reciting the use of a 2-hydroxypropyl-β-cyclodextrin. The combined teachings only recite β-cyclodextrin (e.g., see Tabushi et al, page 1020, Table 1, superscript "a" denoting the β-cyclodextrin concentration at "$5 \times 10^{-2}$ M"; see also column 2, paragraph 1).

However, Castillo et al teaches the following limitations that are deficient in Tabushi et al:

For ***claim 10***, Castillo et al (see entire document) teaches 2-hydroxypropyl-β-cyclodextrin can be used with pharmaceutical formulations (see column 1, lines 27-35).

It would have been obvious to one skilled in the art at the time the invention to use 2-hydroxypropyl-β-cyclodextrin as taught by Castillo in place of β-cyclodextrin as taught by the combined references of Szente et al., Tabushi et al. and the specification because Castillo et al disclose that the 2-hydroxypropyl-β-cyclodextrin is useful in pharmaceutical preparations, which would encompass the phenolic libraries disclosed by

Tabushi et al. and Szente et al. and because the structures of β-cyclodextrin and 2-hydroxypropyl-β-cyclodextrin are structurally related (i.e., the references represent analogous art) and thus would be expected to have similar beneficial properties. Furthermore, one of ordinary skill in the art would have been motivated to use 2-hydroxypropyl-β-cyclodextrin with the libraries disclosed by Szente et al. and Tabushi et al. because Castillo et al explicitly states that they are good replacements for β-cyclodextrin (see Castillo et al, column 1, lines 27-35, "There have been a number of attempts to derivative cyclodextrins in order to decrease toxicity or increase solubility. For example, hydroxy-propyl-β-cyclodextrin is a derivative which has been shown to have a relatively low toxicity and a high aqueous solubility as compared to the parent compound, β-cyclodextrin") (emphasis added).

***Response***

17. Applicant's arguments directed to the above 35 U.S.C. § 103(a) rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

**[1]** Applicants argue again that Tabushi does not disclose the subject matter claimed (e.g., see 2/17/2004 Response, page 8, second to last paragraph).

**[2]** Applicants argue that Tabushi is directed to vitamin K and Castillo is directed to preservatives (e.g., see 2/17/2004 Response, page 8, last paragraph) and, as a result, the references would not be combined.

**[3]** Applicants argue that nowehere does Castillo disclose a library with at least 100 compounds (e.g., see 2/17/2004 Response, page 9, paragraph 1).

**[4]** Applicants argue that Tabushi does not disclose the compound libraries covered by claims 1 and 4-11 (e.g., see 2/17/2004 Response, page 9, paragraph 2).

This is not found persuasive for the following reasons:

**[1]** The Examiner contends that to the extent that Applicants arguments are repeated said arguments were adequately addressed in the response above.

**[2]** To the extent that Applicants are arguing that the references do not represent analogous art, the Examiner contends that Tabushi et al. and Castillo et al. do represent analogous art because the both use cyclodextrin to protect compounds from degradation.

**[3]** In response to applicant's arguments against the Castillo reference individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

**[4]** The Examiner contends that Szente et al. do disclose a compound library with >100 compounds and, as a result, Applicants arguments are moot for claim 1. In addition, the Examiner respectfully disagrees with Applicants that there is no motivation to protect larger libraries with cyclodextrin because it would always be obvious to protect as many compounds from degradation as possible. In addition, Applicants admit in their specification that libraries of

greater than 10,000 compounds were routinely screened in the art at the time of filing and, as a result, a person of skill in the art would be motivated to protect larger libraries for screening purposes, which is exactly what the libraries disclosed by Szente et al. (i.e., screening for taste) and Tabushi et al. (screening for pharmaceutical activity) are used for.

### *Conclusion*

Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (571) 272-0811.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
April 19, 2004

BENNETT CELSA
PRIMARY EXAMINER